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Thesis

"Heredity of the Blood Groups"

by

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TABLE OF CONTENTS

TABLE OF CONTENTS (Cont'd)

Tables and Figures. (con't.)

INTRODUCTION

Brief History. The accumulation of knowledge concerning the heredity of the blood groups, as such, has been confined to a relatively short period of time. However, the knowledge of blood, without considering it as divided into groups and types, began in early times and gradually reached that point whereby its differentiation into groups was justified. The importance and acceptance of this differentiation can be attested to both by its medical and medicolegal applications.

As far back as man can reach in the annals of time the use of blood as a therapeutic measure was advocated, some people believing that the blood was the seat of the soul as well as carrying the vital forces of the body. Thus Pliny and Celsus describe the custom of the people who rushed into the arena to drink the gushing blood of dying gladiators.

As the centuries fled, the people of the Middle Ages gradually came to believe that they could be rejuvenated by drinking the blood of young and healthy youths. The transfusion of blood from three boys into Pope Innocent VIII, in 1419, was probably of this nature.

Approximately one century later the possibility of transferring blood directly from one person to another was suggested by Hieronymus Cardenus (1505-'76) and Magnus Pegelius. The

INTRODUCTION

Major problem. The association of Swaziness consequently the identity of the Nguni groups, as such, has been evaluated to a relatively short period of time. However, the importance of blood, without considering it as direct lineal descent and kinship, seems to have been a primary factor. This paper shows how differentiation into groups was instituted. The development and acceptance of this differentiation can be assisted to hold by the political and ideological applications.

As far back as our own record is the remote or time has one of blood is a phenomenic measure was advanced, some people believed that the blood was the seat of the soul or will to direct the vital forces of the body. Some Ngiy and Cuiba describe the souls of the people who walked into the dreams to denote the general idea of being physicians.

In the medicine field, the people of the Nguni also generally came to believe that they could be rejuvenated by injecting the blood of young and healthy people. The transfer of blood from young body into poor immunent ill. In 1919, was commonly of this nature.

Approximately one century later the possibility of transfer blood directly from one person to another was suggested by Clemmens Gaulmes (1800-1871) and Samuel Wagning. The

exact method by which the transference was to have been carried out is not known. Furthermore, this was suggested only as a possibility and whether or not these authors actually expected their suggestion to be carried out is rather doubtful.

Probably the first person to advocate actual blood transfusion was Andreas Libavius. He wrote in 1615: "Let there be a young man, robust, full of spirituous blood, and also, an old man, thin, emaciated, his strength exhausted, hardly able to retain his soul. Let the performer of the operation have two silver tubes fitting into each other. Let him open the artery of the young man, and put it into one end of the tube, fastening it in. Let him immediately after open the artery of the old man, and put the female tube into it, and then the two tubes being joined together, the hot and spiritous blood of the young man will pour into the old one as it were from a fountain of life, and all of his weakness will be dispelled." (Wiener, 1935, page 36). Whether this experiment was ever carried out by Libavius is still in doubt, but at least he describes blood transfusion which actually has been used and which until lately was the most common method.

"The actual history of blood transfusions and of the science of the blood groups should be dated from the discovery of the circulation of the blood by Harvey in 1616, and the publication in 1628 of his immortal monograph, "Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus." (Wiener, 1935, page 36).

Following this came the first actual blood transfusion which was performed on dogs by Richard Lower in 1665. He exsanguinated dogs and kept them alive by transferring to them, the recipients, blood from other dogs, the donors. His method consisted of connecting the carotid artery of the donor to the jugular vein of the recipient. The connection was made by means of quills. As can be seen, although the method was crude, it does not differ essentially from methods used two hundred and fifty years later.

The first actual case of transferring blood into a human being was performed in 1667 by Denys and Emmerez. These two men successfully transferred nine ounces of blood from the carotid artery of a lamb into the vein of a young man. Encouraged by the success of this experiment Denys performed several similar operations. On his fourth transfusion the patient died and from this resulted the first setback in the progress of blood transfusion. A French court decreed that the performance of this operation was to be prohibited in the future except under the sanction of the Faculty of Medicine.

For a period of one hundred and fifty years nothing more was done in regard to this practice. Finally, however, James Blundell attempted to revive it. He did so to lessen the number of deaths, especially those of midwifery. His method was even cruder than Lower's, but it served as a stimulus which awakened the interests of the profession in blood transfusion.

Following this case, the first lateral thoracotomy which was performed on a boy in January 1949, in Lima, exsanguinated both and kept them alive by transfusion in spite the hemolysis, blood from other boys, the donors. His method consisted of connecting the arterial system of the donor to the jugular vein of the recipient. The connection was made by means of tubes. It can be seen, although the method was crude, it does not differ essentially from methods used for complete and first-rate later.

The first series of cases of transaortic-line blood transfusion was performed in Lima by Dorre and Sabiston. Their dog was successfully transfused with quarts of blood from the abdominal veins of a dog into the vein of a second dog. In conjunction by the success of this experiment they performed several cardiac operations. In six cases transfusing the patient died and from this resulted the first refusal in the progress of blood transfusion. A Russian group therefore last the performance of this operation was to be prohibited in the future except during the execution of the theory of medicine.

For a period of one hundred and fifty years nothing more was done in regard to this problem. Finally, however, Levin finally attempted to revive it. He did so in lessen the number of deaths, regardless some of modifiers. His method was from another than Lewis. But it serves as a stimulant which awakened the interests of the professions in blood transfusion.

Through the efforts of many workers, too numerous to mention, the operation of blood transfusion was gradually perfected until today it is a safe and invaluable therapeutic procedure when performed by trained surgeons.

The Problem of the Thesis. Before this state of perfection could be reached certain difficulties had to be overcome. 1) Difficulties caused by the coagulation of the blood had to be prevented by perfection of the transfusion apparatus and technique. 2) Unfavorable reaction to transfusion caused by "incompatibility" of the blood of the donor and the recipients had to be recognized and methods of preventing these reactions had to be devised.

The first of these difficulties will not be discussed in this paper because it deals more with the mechanical factors rather than with the scientific principles involved. However, it can be stated here that this difficulty no longer exists due to the rapid strides which scientific equipment has taken in the direction of perfection.

The answering of the second difficulty naturally leads to the causes of the incompatibility and also to the "why" of the difficulty. This, of course, can only be answered by referring directly to the mechanism, or mechanical factors, controlling the heredity of the blood groups.

It should be stated here that Lower ran into difficulties when he tried blood transfusions. He found that blood of domesticated animals, transfused into man, was often followed

by hemoglobinuria (black urine), fever and even death. Panum and Landois found that although an exsanguinated animal could be kept alive with blood from an animal of the same species, it would die if blood of an animal of a different species was used. Landois showed that if human blood was mixed "in vitro" with the blood of animals the white blood cells would lose their amoeboid motion and die, and the erythrocytes would become hemolyzed. (Wiener, 1935)

These works, however, did not explain why transfusions in man should be followed by dangerous or fatal reactions. The failure to answer this question almost caused the complete abandonment of the technique. It was not until 1900 that Landsteiner finally explained the phenomena observed by showing that the serum of a normal person could agglutinate or hemolyze the blood of certain other people. This was, perhaps, the most important single discovery related to blood transfusion and was the basis for the science of the blood groups.

The inheritance of these blood groups was finally satisfactorily explained by Bernstein. Other scientists also attempted to explain the mechanism controlling the heredity of blood groups but Bernstein's theory agrees more with the facts and thus is the accepted theory of today. (Wiener, 1935).

Further investigations, by Landsteiner and Levine (1926) led to the discovery of the so called "M" and "N" types. These men also put forth the most promising theory in regard to the heredity of these types.

to commutators (blood types). Fisher and Ford [illegible]. Snow and landsin found that although in [illegible] [illegible] be kept alive with blood from an animal of the same species, it would die if blood of an animal of a different species was used. Landsin showed that if human blood was mixed "in vitro" with the sera of animals the white cells would [illegible] [illegible]-mechanical action and die, and the erythrocytes would become [illegible]. (Simmons, 1934)

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The introduction of sodium citrate which finally made relatively safe transfusions by possible. Other scientists also attempted to solve the problem concerning the compatibility of blood groups but Ferrebee's theory seems more sound and close to the accepted theory of today. (Simmons, 1934).

Further investigations, by Jansky and Lewin [illegible] led to the discovery of the so called "a" and "b" types. These can also be used to provide the most probable theory in regard to the matter of human types.

Further differences have been observed to some extent by other scientists, but the facts that are now known do not warrant a further subdivision. Some scientists postulate, however, that there are so many divisions of the blood that eventually an examination of the blood of a person will be as accurate as the finger printing of that person is today. In other words, the blood of each individual is probably different from all others. Of course, no proof of this statement can be offered, but it certainly is not an impossibility.

THE FOUR BLOOD GROUPS

Blood Groups in Rabbits. Before delving directly into the mechanism controlling the heredity of the blood groups of man, certain conditions of the blood must be understood. Experiments carried on with the blood of rabbits serve as an admirable indicator for the general behavior of blood. It may be stated here that while the mechanism of inheritance and agglutination appears to be the same in man and rabbits, the agglutinative substances are different. As can be seen this does not detract from the comparison in general but care must be taken when treating the agglutinogens and agglutinins controlling the reactions.

In both human beings and rabbits agglutination or hemolysis results from a two-fold agency consisting of (1) an agglutinogen carried in the red blood cells of the donor, and (2) an agglutinin carried in the blood plasma of the recipient. Both of these factors must be present in order that the clumping of the blood cells will occur. In other words, if agglutinogen "A" is present in the blood cells of the donor but the corresponding agglutinin "a" is not present in the plasma of the recipient no agglutination will result.

Of course, the opposite case would be true. That is, the plasma of the donor, if it has the same or corresponding agglutinin, can cause the clumping of the erythrocytes of the

The Blood Group Genes

Blood Groups in Medicine. Before entering directly into the genetics (mendelian) the normality of the blood groups of man, several conditions of the blood must be considered. Hemolysis resulting in with the blood of relative ease is an economic hindrance for the general laboratory of blood. It may be stated here that while the mechanism of hemagglutinin and agglutination reactions be in the blood in man and animals, the agglutination reactions are different. It can be seen that does not interest from the transfusion in general but also that be taken place involving the laboratorians and individuals concerning the medicine.

In this study medical and public administration or immediate results from a non-type agency consisting of (1) an agglutinogen activity in the red blood cells of the donor, and (2) an agglutinin material in the blood plasma of the receiving. Each of these factors must be present in order that the clumping of the blood cells will occur. In other words, a agglutinogen "A" is present in the blood cells of the donor the nonexistence of the agglutinin "a" is not present in the plasma of the receiving or agglutination will occur.

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recipient.

One of the simplest ways to picture agglutination or the lack of it, is through the Ehrlich symbols. These symbols represent an agglutinogen as a receptor cavity in a blood cell into which will fit only a similarly shaped agglutinin. This fitting together of similarly shaped parts designates that agglutination occurs; where dissimilar portions will not unite denotes lack of agglutination or hemolysis.

In Figure A is shown the Ehrlich symbols to designate the known agglutinogens and agglutinins of rabbits. These, of course, do not show the nature of the agglutinogens or what actually occurs in agglutination, yet they are worth while because they do show a relation which exists between agglutination and its causes.

From the work of C. E. Keeler and W. E. Castle (1934), who performed most of the experiments leading to knowledge of blood groups in the rabbit, it is found that there are four blood groups now recognized in this animal. These four groups are classified as follows:

1. Blood cells containing no agglutinogens. This group is called the zero group and cannot be agglutinated by any known agglutinin.

2. Blood cells containing "H_1". These cells are agglutinated by serum containing agglutinin "h_1", but serum containing "h_2" has no effect. This group is known as the "H_1" group.

3. Blood cells containing "H_2" agglutinogen. These cells

are agglutinated by serum containing "h_2", but serum containing "h_1" has no effect. This group is called "H_2" group.

4. Blood cells containing "H_1 H_2" agglutinogens. These cells are agglutinated by serum containing either "h_1" or "h_2" agglutinins. This group in turn receives the name of the agglutinogen present, that is, the "H_1 H_2" group.

(Figure B shows what occurs when these four groups are brought in contact with serum of either "h_1" or "h_2").

One important fact was discovered by Keeler and Castle (1934) in regard to the agglutinins. Upon examination and experimentation with untreated blood, it was found that the agglutinins were not present in sufficient numbers to cause agglutination of any foreign blood. Whether the agglutinins were present at all could not be determined but it was found that their presence could be stimulated or artificially induced by the introduction of blood cells containing an agglutinogen not present in the cells of the recipient. In these cases the corresponding agglutinin arose as an immune reaction. (Keeler and Castle, 1934).

To make the above statement clearer a very simple case will be examined. If a "zero" rabbit is injected with the blood from group "H_2" the corresponding agglutinin "h_2" will be produced in the serum of the "zero" rabbit. Now if this serum is injected into an "H_2" rabbit agglutination will result.

The mechanisms controlling the heredity of these groups have been studied and the results seem to indicate that the

agglutinogens are transmitted as dominant unit characters, "H_1" and "H_2". These also appear to be allelomorphic.

In Figure C are shown four crosses which support the theory of Keeler and Castle (1934).

Cross 1 proves definitely that "H_1" is a dominant unit character, having in the "F_2" generation a ratio of 1:2:1.

Cross 11 shows the same results as above, denoting that "H_2" is also a dominant unit character.

Cross 111. Here two homozygous animals of "H_1" and "H_2" are crossed and the "F_1" generation gives only a heterozygous animal. This is taken as proof that the agglutinogens "H_1" and "H_2" are autonomous.

In Cross IV a heterozygous animal ("H_1 H_2") was crossed with a "zero" rabbit. The results, as seen in Figure C, show that "H_1 H_2" individuals transmit "H_1" and "H_2" in separate gametes, since when mated with a "zero" individual only heterozygous "H_1" or "H_2" offspring are produced. In other words, "H_1" and "H_2" are allelomorphs.

Although this latter statement is true neither one of the agglutinogens affect the action of the other. That is, each one produces its specific antibody regardless of whether the other is present or not. Proof of this statement was definitely established by the above mentioned authors when they made sixteen different sorts of blood transfers. Their conclusions are as follows:

multiplication are transmitted by dominant only alternatives. "g_1" and "g_2". These also appear to be allelomorphs.

In figure 2 are shown four crossing which involved the Green of Rabbit and Albino (Ccrr).

Green I (white variability) has "g_1" in a heterozygous condition, leaving as the "g_2" recessive a white or albino.

There is never the slow reversion to white. Dominant Green "g_1" is also a recessive with albinism.

Cross III. When the homozygous albino or "g_2" and "g_2" are crossed and then "g_1" heterozygous green or a heterozygous white. This is done so that then the allelomorphs "g_1" and "g_2" are determined.

In cross IV a homozygous albino ("g_2 g_2") was crossed with a "pure" rabbit. The result, as seen in figure 2, was that "g_1 g_1" individuals resembled "g_1" and "g_2" in appearance, hence also white with a "pure" individual with heterozygous "g_1" as "g_2" affecting the producer. In other words, "g_1" and "g_2" are allelomorphs.

Although this latter statement is true without use of the allelomorphic effect the action of the other. That is, each one possesses its specific inherent properties of quality- the albino is weaker or sor. Just as this statement all variability is attributed by the above mentioned quality when they each showed different sorts of Dominant characters. Their characteristics are as follows:

1. "Univalent serum (containing either "h_1" or "h_2") results in six out of seven categories of blood transfer expected to yield positive results." (Keeler and Castle, 1934)

2. Serum containing both "h_1" and "h_2" agglutinins results when "H_1 H_2" blood is injected into a"zero" rabbit (a mixture of "H_1" and "H_2" blood would give the same results).

According to these two conclusions it would seem that by proper injections incompatibilities in the blood of the foetus could be produced. This seemed more probable when it was found that agglutinins formed in the mother's blood passed freely through the placenta into the blood of the young in the uterus. This was shown by injecting a "zero" female with "H_1 H_2" blood and thus producing "h_1" and "h_2" agglutinins in her blood plasma. This female was then mated to a "zero" male. Naturally, the offspring were also of the "zero" group, but their serum contained the "h_1" and "h_2" agglutinins. These could have come only from the blood of the mother.

From this it would seem possible to produce incompatibilities in the blood of the foetus. This was actually tried by Keeler and Castle (1934) and the exact method is given here. A "zero" group mother was injected with blood from an "H_1 H_2" donor and thus "h_1" and "h_2" agglutinins were built up in her blood. The mother was then mated to a buck of "H_1" group. Obviously, the mother had agglutinin "h_1" which would be antagonistic to any agglutinogen borne by half of her young through inheritance from the father. Since it has been shown

that the agglutinins pass freely through the placenta into the young in the uterus, then theoretically, agglutination should occur in all those young receiving the "H_1" from the father. The results, however, showed that in three such litters, including fourteen individuals, there were nine individuals having incompatible erythrocytes but no agglutination or any other harmful results took place. This seems to show that some protective medium was produced to offset the fatal results which were expected.

Blood Groups in Man. Before treating of the inheritance of blood groups in man it would be well to pause for a moment and analyze the nomenclature that has been used to designate the four different blood groups. The most important of these are as follows: Moss, Jansky, and the International Nomenclature. The latter is officially recognized by the Health Committee of the League of Nations.

The Moss and Jansky numberings are no longer used in scientific publications but are still used in a number of institutions. In both of these, numbers 11 and 111 are alike but Jansky's number 1 group is Moss's number IV and vice versa. As can be seen, this resulted in confusion on many occasions and has probably been responsible for some very serious accidents.

It was to overcome such accidents that the International Nomenclature was brought into use. This system is based on the mechanism controlling the heredity of the blood in each

group which in turn brings out the actual agglutinogen content of the blood. Thus we have the following groups: "O", "A", "B", "AB".

This naturally leads to the relation that exists between the agglutinogens and the agglutinins. A very simple rule formulated by Landsteiner shows the exact relationship.

"Only those agglutinins are present in the serum for which there is no corresponding agglutinogens in the erythrocytes." (Wiener, 1935). For example; the serum of a group "A" individual contains only agglutinin "beta", not agglutinin "alpha". This of course, serves as an admirable check on the presence or absence of the agglutinogen.

Heredity of the Groups. Three main theories have been presented to explain the exact mechanism of heredity of the agglutinogens "A" and "B". Von Dungern and Hirschfeld thought that "A" and "B" were inherited independently of each other, and that their inheritance depended on two independent pairs of allelomorphic genes. In 1924 Bernstein showed that this theory did not conform to the facts and postulated his theory in which the inheritance of the agglutinogens depended upon three allelomorphic genes, A, B, R. A third theory was proposed by Kirihara and Haku and was a sort of compromise of the two above mentioned theories. It was based on a theory of linkage. (A diagram showing the relation of these theories is represented in Figure D.)

At present all investigators, even Hirschfeld himself,

group which is then taken out the actual equivalence classes of the final. Thus we have the following groups: "a", "b", "c", "d", "ab".

This naturally leads to the relation that exists between the equivalence and the equivalence. A very clearly was formulated by Lambek where he said "Recall.

"Only those equivalences are present in the form for which there is no corresponding equivalence in the equivalence." Lambek, 1961. For example, the group of 4 group "a" includes "ab" only equivalence only equivalence "ab", not equivalence "abc" this or "cabc" exists if an equivalence exists on the equivalence or equivalence of the eq equivalence.

Equivalence of the equivalence. There were equivalence have been presented to explain the least equivalence of equivalence of the equivalence "a" and "b". The equivalence the equivalence equivalence "a" and "b" have equivalence equivalence or equivalence equivalence, and then equivalence equivalence equivalence on two equivalence equivalence of equivalence equivalence. In this equivalence equivalence that there lie our equivalence to the equivalence and equivalence equivalence in which the equivalence of the equivalence equivalence equivalence there equivalence equivalence. e. g. "a". A point equivalence has given rise by Kleiman and there and has a set of equivalence of the the above equivalence equivalence. It has been as a theory of lineage. It depends upon the equivalence of equivalence equivalence to equivalence equivalence.

It appears all equivalence, even equivalence equivalence.

agree that Bernstein's theory is correct. However, in order to understand the theory, and the reasons for its acceptance, it was thought advisable to discuss the original theory of von Dungern and Hirschfeld.

According to this theory the heredity of the agglutinogen "A" depends upon a pair of allelomorphic genes, "A" and "a", where "A" is dominant over "a". In regard to agglutinogen "B" the same mechanism holds true, that is, a pair of allelomorphic genes, "B" and "b", with "B" dominant over "b". The possible genotypes and phenotypes of the four blood groups according to this theory is given in Table I. (Wiener, 1935)

, According to this table if the agglutinogen alone is considered only two phenotypes are possible; individuals possessing agglutinogen "A" (designated as A+) and those lacking the agglutinogen (considered as A-). Also we find that three genotypes are possible, namely, "AA","Aa", "aa". The first two of these genotypes will possess the agglutinogen "A", whereas the individual possessing "aa", will lack this agglutinogen.

Naturally the genotypes cannot be ascertained as such (due to lack of serological methods) and thus only the phenotypes are observed. In other words, it makes little difference to the average practitioner or laboratory technician whether the person is "AA" or "Aa".

Following Mendel's laws therefore, these genes can be transmitted to the offspring only if they are present in at least one

of the parents. The same law, of course, holds true for agglutinogen "B".

Since 1910, more than fifty independent workers have made studies on the heredity of the blood groups and only a small percentage of apparent exceptions were found. These exceptions however, appeared in the early studies and may be properly attributed either to faulty technique or to illegitimacy. However, it can be safely said, for the opinion of these scientists is unanimous, that "there is not a single completely proven exception to the law that the agglutinogens "A" and "B" cannot appear in the blood of a child unless present in the blood of one or both parents." (Wiener, 1935)

Statistical Considerations. The most obvious fault of this theory of Hirschfeld is that it does not conform to the expectancies of all possible crosses. This is especially true in those crosses involving group "AB". According to this theory a cross between group "O" (genotype aabb) and Group "AB" (genotypes AABB, AaBB, AABb, and AaBb) should produce all possible groups; namely "O, A, B, AB". This follows from the fact that group "O" (aabb) can only produce gametes with genes ab, whereas, group "AB" can produce gametes of the following types; AB, Ab, aB, and ab. Thus random unions of these gametes would produce zygotes with the following genotypes; AaBb, Aabb, aaBb, and aabb. The phenotypes of these would then be "AB, A, B, O".

This same result should appear in all other possible

of the matrix. The case lies, of course, quite near the ex-
ceptional case "P".

Since this, also like fifty intermediate matrices here have
relation on the basicity of the "low" groups are only a small
percentage of possible transitions were found. These exceptions
however, showed in the very minutes and may be reasonably ex-
plained either by finite statistics or in biological theory. Con-
ver, it may be strongly said, for the opinion of these exceptions
is unknown. Only there is not a single consistently wrong re-
sult. In the one case that has exactly matrix "P" and "Q" cannot
occur in the stem of a single mutant present in the blood of
one of each parent. (Gibson, 1943)

Statistical considerations. The most serious fault of
this theory of inheritance is that it does not produce in the
experiments of all possible results. This is especially true
in those crosses involving group "AB". According to this
theory a cross between group "A" homozygote blood and group "B"
(heterozygote blood, AB0, AB0) and AB0 should produce all pos-
sible groups namely "A", "B", "AB", "O". This follows from the
fact that group "O" (AB0) can only produce gametes with genes
A0, respectively. Thus "AB" can produce gametes of the following
types: AB, AB, A0, A0. But another matrix of these genetic
model produce results with the following proportions: AB, AB,
A0, A0. The proportions of these would then be "1:1:
1:1".

This case exactly should appear in all other possible

crosses involving group "AB". To show how this follows, a cross between group "A" and group "AB" will be examined. Group "A" has one possible genotype of Aabb and group "AB" has a possible genotype of AaBb. Thus in gamete formation two types will be produced from group "A", namely, Ab, ab; and four types will be produced from group "AB"; namely, AB, Ab, aB, and ab. Thus random mating will result in the formation of AABb (phenotype "AB"), Aabb (phenotype "A"O, aaBb (phenotype "B"), and aabb (phenotype "O"). This same result is possible from all other crosses since in all cases the recessive characters ab are capable of being formed.

If this relation did hold then a corresponding relation should exist between the frequencies of the genes "O, A, B, AB". Hirschfeld claimed that this relation did exist. Wiener (1935), and Wiener, Lederer, Poloyes (1929), in order to check on the frequencies of these genes according to Hirschfeld's theory, determined the relationship that should exist between the genes. The formula that these men derived is as follows; $\bar{O} \times \overline{AB} = \bar{A} \times \bar{B}$, where $\bar{O}$, $\bar{A}$, $\bar{B}$, $\overline{AB}$, represent the frequencies of the genes.

From statistical evidence obtained from the most prominent men in this field, it has been found that in the vast majority of cases this relation does not hold. Therefore, the theory that the agglutinogens "A" and "B" are inherited independently of one another must be false.

In regard to the theory of Kiruhara and Haku "as Bernstein

pointed out in his original paper, the only effect of linkage would be to delay the attainment of equilibrium. In homogeneous populations the relation $\bar{O} \times \overline{AB} = \bar{A} \times \bar{B}$ should also hold under such an hypothesis. It is, therefore, apparent that the theory of linkage is open to the same objections as the theory of von Dungern and Hirschfeld." (Wiener, 1935, page 95)

The Bernstein Theory. Instead of two pairs of allelomorphic genes, Bernstein postulates three, "A", "B" and "R". In this case "A" and "B" are dominants and "R" is a recessive character. At least one of these genes is present in each member of a chromosome pair so that each somatic cell contains two genes but each sperm or ovum contains only one. (Wiener, Lederer, Poloyes, 1930). This type of heredity is not uncommon and has been called "multiple allelomorphism." Since each germ cell contains only one of the three genes "A", "B", and "R", from combinations of these three possible kinds of ova and sperm it is possible to find six different genotypes. These various kinds are shown in Table XII as are their corresponding phenotypes.

Since the agglutinogens "A" and "B" are inherited as Mendelian dominants, they cannot possibly appear in a child unless present in at least one of the parents. In this respect Bernstein agrees with von Dungern and Hirschfeld. However, if either parent belongs to group "AB", then his or her genotype will be "AB". Therefore, the germ cells will contain either "A" or "B". Since this is true it would be impossible for any

"O" child (RR) to be produced by any "AB" parent since the only possible genotypes are "AR" and "BR". Conversely, an "O" parent cannot give rise to an "AB" child. (Wiener, Lederer, Poloyes, 1930).

In regard to the statistical consideration of Bernstein's theory, it can be said that all the results appear to justify its claims in regard to the frequencies of the genes.

Comparison of Hirschfeld and Bernstein's Theories. The exact comparison of these two theories can be found in Table XI. As can be seen, the expectancies are identical in all but but the last four cases. Actual facts agree with the Bernstein theory in these cases. Hence, it appears that what is considered as accidental by Hirschfeld is considered as inevitable by Bernstein.

This statement can be definitely proved by considering the figures presented by Wiener, Lederer and Poloyes in 1930:

1. Ninety-four "AB" families with one hundred and forty-two children were examined. None of the offspring were of group "O".

2. Four hundred and eighty-five "O" mothers were examined. Of the five hundred and sixteen children not one was of group "AB".

According to Hirschfeld's theory there should have been at least thirty-four exceptions. Bernstein's theory on the other hand predicted exactly what was found.

It is upon such overwhelming evidence as this that there

"u" would (1a) to be measured by any "u" effect which the [illegible] possible experiments are "u" and "v". Conversely, an "u" effect cannot give rise to an "u" cause. Stoner, Leonard, Malgren, 1964).

In terms of the statistical probabilities of quantum theory, it can be said that all the possible events in nature are origin in the fundamentals of the world.

Conversion of Liquefied Gas Condensate Cylinders. The result conversion of single the Russian can be found in Table 2. As a to be seen, the experiments are inclined to all out not for just four cases. Lower fuel equipment can generate lower in three cases. Lower, it appears that what is achieved as acceleration in [illegible] is compensated as lowering of power.

This statement can be definitely proved by considering the figures presented by Stoner, Leonard and Malgren in 1980:

1. Ninety-four "u" results with the burned and fuel-injection engine measured. None of the oil-engine were of group "u".

2. Four unburned and eighty-five "u" results were obtained. In the five burned and eighteen results not one was of group "u".

According to Kirchhoff's theory there should have been at least fifty-four results. Experimental theory on the other hand predicted exactly what was found.

It is even also experimental evidence as this that there

is a unanimous acceptance of the Bernstein theory regardless of the certain "exceptions" which appear to be found.

That those exceptions have appeared cannot be denied but a comparison of the number of cases found before and after Bernstein's theory was published reveals a remarkable decrease during the latter period. Previous to its publication in 1926, the exception to the cross of "B" X "AB" was 26.6%. After 1926 the percentage dropped to 3.18%. Similarly in a cross of "A" X "AB" there was a decrease of from 3.77% to .87%; and in the "B" X "AB" families the number of exceptions dropped from 11.11% to .83%.

The sudden decrease in the percentages of these "exceptions" has been explained by Wiener, Lederer, and Poloyes (1929), (1930). They claim that these cases were not considered as exceptions until after Bernstein's publication. They also claim that the so-called "exceptions" were due mainly to (a) faulty technique, (b) failure to test a sufficient number of people, (c) errors in computation, (d) failure to study a homogeneous group, (e) and selection of a sub-group for study which is not representative of the entire group.

In conclusion, then, the acceptance of the Bernstein theory has been justified, and therefore, so also have the two laws which have been drawn directly from it. These laws have already been mentioned but not worded as such.

1. The agglutinogens "A" and "B" cannot appear in the blood of a child unless present in at least one of its parents.

2. A parent belonging to group "AB" cannot give rise to a group "O" child, and a group "O" parent cannot give rise to a group "AB" child.

Heredity of the Agglutinins. So far only the agglutinogens have been considered. Obviously, there must be some relation existing between the agglutinogens and the agglutinins. It has already been shown that the agglutinins are present in the serum of an individual for which there is no corresponding agglutinogen in the erythrocytes. Therefore, it can be said that the heredity of the agglutinins depends somewhat on the heredity of the agglutinogens. This, however, fails to account for the reciprocal relationship.

Two theories have been advanced which adequately account for this heredity.

1. According to Bernstein all individuals produce both "alpha" and "beta" agglutinins. This theory is based on the fact that the agglutinins developed later than the agglutinogens. Bernstein's explanation, as given by Wiener (1935) is as follows: In an individual of group "A", first the agglutinogen "A" will appear. When the agglutinins are now elaborated, the former agglutinin will be absorbed by the agglutinogen "A".

2. Furuhata, on the other hand, explains this heredity by two pairs of allelomorphic genes, "A" and "a", and "B" and "b".

"A" determines the appearance of agglutinogen "A".

"a" " " " " agglutinin "a" .

"B" determines the appearance of agglutinogen "B".

"b" " " " " agglutinin "b".

According to this theory, these genes are transmitted in three completely linked pairs, "Ab," "aB", "ab". This, of course, corresponds to the genes "A", "B", and "R", of Bernstein. Consequently, they yield the same results as that of Bernstein.

The only difference between the two theories just enumerated lies in the fact that in Bernstein's theory incompatible agglutinins are formed and then eliminated. These incompatibilities do not appear according to Furuhata. The determination of which of these two is the more accurate seems to lie in the fact that Bernstein's is more general and thus seems to account for all types, whereas, Furuhata's fails to account for the occurrence of anomalous agglutinins in the sub-groups of "A" and "AB". For this reason preference is given to Bernstein's theory. (Wiener, 1935)

SUB-GROUPS OF GROUP A AND GROUP AB.

In 1910, von Dungern and Hirschfeld reported that when a group "B" serum was absorbed by a group "A" blood, until it lost its power to agglutinate the absorbed blood, the serum still retained its power to agglutinate certain other types of Group "A" and "AB". On this evidence they suggested a subdivision of group "A" and group "AB".

This phenomenon is apparently caused by two agglutinins: alpha, which acts on certain agglutinogens, namely, all groups of "A" and "AB"; and alpha 1. which acts only on a majority of group "A" and group "AB", namely those belonging to sub-group "A_1" and sub-group "A_1 B". Bloods that do not react with the absorbed group "B" serum belong to the so called sub-group "A_2" and sub-group "A_2 B". (Wiener, 1935)

Nature of the Sub-groups. The reactions observed above have been explained by three different methods:

1. By assuming the existence of an additional agglutinating substance "A_1", in sub-group "A_1", besides the agglutinogen "A" which is common to both the sub-groups. (Landsteiner and Witt, 1926)

2. By assuming the existence of two qualitatively different agglutinins. "The existence of two qualitatively different sub-types in Group II blood is confirmed with the method

of cold agglutination. Two cold agglutinins are shown to be present in Group II sera, one of these acting on bloods "AA_1" and the other on bloods "AA_2" ." (Landsteiner and Levine, 1926). This, of course, also shows that there are tow agglutinogens present, namely, "A_1" and "A_2", in the two sub-groups.

3. By assuming a purely quantitative difference, that is, caused by varying the amount of the same agglutinogens in the two sub-groups. Lattes and Cavazutti (1926) particularly hold this, and do so because they found that if a group "B" serum, which contained both alpha and $alpha_1$, were mixed with an excess of "A_2" blood, all the agglutinins would be removed.

On the other hand, Landsteiner and Witt (1926) have presented evidence which they believe to be conclusive proof of the qualitative differences existing in the sub-groups. Wiener (1935) explains this proof offered by the above mentioned authors: "By the method of splitting off agglutinins, two fractions of agglutinin were separated from group B solutions. One (split off from blood of sub-group "A_2") agglutinated both "A_1" and "A_2" blood to nearly the same titer; whereas, the other (split off from sub-group "A_1") did not act on "A_2" blood although agglutinating "A_1" blood not much less than the first agglutinin solution."

This was taken to be proof of the existence of two different agglutinins, alpha and $alpha_1$. Landsteiner (1926) further explained this theory by assuming the existence of two

of cell isolations. The cold sensitivities are shown to be genetic, in there is zero, one or three genes controlling "cold" and the other is closer "cold". (Brandham and Dawkins, 1971). Note, of course, also some cold sensitive are low or intermediate versions. Usually, "g" and "h" in the two genotypes.

2. By assuming a simple quantitative model, one can, in order to explain the amount of the good heterozygotes in the F2 sub-genotypes. Lewis and Dawkins (1970) particularly said this, and in it because they found that if a strong "c" genotype cold sensitive have alone and alone, then along with an increasing of "c" blood, all the heterozygotes would be resistant.

In the other word, Dawkins and Wild (1971) have proposed multiple-gene hypothesis to be responsible for genetic of the qualitative differences existing in the strains.

Lewis (1970) explains that being affected by the genes controlling of allele. By the method of separation off equivalent, two fractions of cold-sensitive were separated from cross "c" resistance. The (with off from alone or non-cross "c") heterozygote had "g" and "h" blood to exactly the same level; however, the other (with off from non-cross "g") did not had as "g" blood although different haplotypes "g" blood are more than the "h" haplotypes solution."

This can lead to be proof of interactions of two gene-F2 sub-genotypes alone and alone. Dawkins (1969) Lewis suggests that theory by looking the relationship of the

qualitatively different agglutinogens, "A_1" and "A_2". According to this "A_1" reacts more strongly with alpha than with $alpha_1$; and "A_2" reacts less intensely with alpha than "A_1" and only feebly with $alpha_1$.

Thomsen, on the other hand, who has presented the most acceptable theory in regard to the heredity of these sub-groups, claims that the agglutination does not depend upon the existence of qualitatively different agglutinogens in the sub-groups. He explains the same phenomena observed by Landsteiner by assuming that the so-called agglutinin $alpha_2$ may be really an agglutinin acting specifically on group "O" blood, and that it acts on "A_2" cells only for the reason that these "A_2" cells are mostly heterozygous (genotype "A R") and thus contains the factor "O". This theory is based on the fact that the $alpha_2$ sera agglutinates very strongly the "O" group and agglutinates the "A_2 B" group weakly, if it does so at all. (Wiener, 1935)

As can be seen the actual cause of why the "B" blood which has been absorbed by "A", can still agglutinate other bloods cannot be definitely established. All the theories advanced have some points in their favor, but extensive research must still be made before any definite answer can be given.

<u>Heredity of the Sub-groups</u>. The most prominent theory advanced in regard to the heredity of these sub-groups was presented by Thomsen, Friedenreich and Worsaae. This theory postulates, instead of three allelomorphic genes (Bernstein's theory), that there are four allelomorphic genes, "A_1", "A_2",

qualitatively different equilibrium. "A_1" and "A_2", according to this, "A_1" reacts more strongly with alum than with alum; and "A_2" reacts less strongly with alum than "A_1" but still reacts with alum.

However, on the same day, one has produced the same antiserum strongly in excess to the quantity of these antigens, rather than the equilibrium does not depend upon the existence of qualitatively different antigenicities in the antigens. In solving the same problem, one may be tempted by assuming that the antiserum equilibrium alone may be really an equilibrium acting simultaneously on group "A" alone, as has on "A_2" which gain for the reason that these "A_2" cells are mainly heterogenous (identical "a a") and hence contains factor "b". This theory is based on the fact that the alone the quantitative view strongly for "b" cause one agglutinates the "A_2" group mainly. If it does so it all. However, this is not to mean the proposed model or why one "b" cause which has been discovered by "b", not still sufficiently other figure ground to definitely be disposed. It has therefore advanced have done prior in that theory, but attempts possible that still be more factors and factors should be given.

<u>Theory of the antiserum</u>. The last theoretical theory answers in regard to the length of time antigens are produced by immune, colonoscopies and serum. This theory qualitative, instead of those qualitatively more (normality) theory, that there are four alimentarium cells, "A_1", "A_2",

"B", and "R". In this case "A_1", "A_2" and "B" are dominant over "R", and gene "A_1" is dominant over gene "A_2". (Wiener, 1935) The possible phenotypes and genotypes, according to this theory, are shown in Table IX.

This theory does not contradict in any way the fundamental principles of Bernstein's theory. However, if this theory is correct the following additional laws should be added to those already given as following logically from Bernstein's theory. (Wiener, 1935).

1. The agglutinogen "A_1" cannot appear in the blood of a child unless present in at least one of its parents.

This rule depends on the fact that "A_1" is dominant over "A_2". Thus, in matings such as "A_2" X "A_2" or "A_2" X "B" etc., all groups "A" and "AB" children must belong to group "A_2" and "A_2 B". On the other hand, matings such as "A_1" X "A_1", "A_1" X "O", etc., both "A_1" and "A_2" children are possible since the genotype of the "A_1" parent might be "A_1 A_2".

2. An "A_1 B" parent cannot give rise to an "A_2" child, and vice-versa. This necessarily follows because an "A_1 B" individual can produce only germ cells of "A_1" or "B". The children must possess at least "A_1" or "B" genes and therefore, the parents cannot give rise to an "A_2" child (Genotypes "A_2 A_2" or "A_2 R"). Conversely then, an "A_2" parent cannot give rise to an "A_1 B" child.

3. In special matings, such as "A_1 B" X "B", and "A_1 B", X "A_1 B", "A_2 B" children cannot result, since one "A_1 B"

individual cannot give rise to an "A_2 B" child unless the gene "A_2" is supplied by the other parent. In these cases neither parent possesses gene "A_2".

4. Where there are a number of children resulting from such matings as "A_1" X "O", "A_1" X "A_1", "A_1" X "B", "A_1" X "A_1 B", and "A_1" X " A_2 B", and one of the children belongs to group "O" or group "B", none of the remaining children can belong to sub-group "A_2" or sub-group "A_2 B", and conversely.

This rule depends upon the fact that if the child is group "O" the genotypes of the "A_1" parent must be "A_1 R", so that "A_2" children could not possibly appear. Similarly, if one child is sub-group "A_2", the genotype of the "A_1" parent must be "A_1 A_2" and group "O" children cannot occur. This is shown more clearly in a cross of "A_1" X "O" where there are only three possibilities:

Parents	Children
A_1 A_1 X RR	A_1 R
A_1 A_2 X RR	A_1 R, A_2 R
A_1 R X RR	A_1 R, RR

Naturally then, when the exact genotypes of the parents are known the value of determining the genotypes is increased tremendously. The genotype of the "A_1" parent can often be determined if the groups (or phenotypes) of the grandparents are known. Thus, if one of the grandparents belongs to sub-group "A_2 B", the "A_1" parent must belong to genotype A_1A_2. On the other hand, if the grand parents belonged to group "O"

or group "B", the "A_1" parent must belong to sub-group "A_1 R". If both grandparents belong to sub-group "A_1 B" the genotype of the parent "A_1" is obviously "A_1 A_1". In all other cases the exact genotype of the "A_1" parent remains uncertain. (Wiener, 1935)

All the available data show that, fundamentally at least, the Thomsen theory is correct. This does not deny the fact that certain inconsistencies have been found, but these seem to have been due to illegitimacy and certain other errors that would be of considerable importance in the final analysis. Wiener (1935) has summarized all the important works on this subject and a brief explanation of these works will be given here.

1. Friedenreich and Zacho, in a study of one hundred and three families with two hundred and eighty-three children, found no exceptions to the rules already mentioned.

2. Landsteiner and Levine found three exceptions to the first rule which appeared to be accounted for by illegitimacy.

3. Thomsen, Friedenreich and Worsaae found one family of "A_2" X "O" with two "A_1" children. This, of course, is contrary to the first rule. This was accounted for by the authors as being due to the weakening of the sensitivity of the "A_2" parent since at the time he was typed he had reached the age of eighty years.

4. Wiener and Rothberg also found three exceptions to the fourth rule in a study of one family, "A_1" X "O". The children

were of group "O", "A_1" and "A_2". These authors claim that technical difficulties could not account for the results. However, even in this case illegitimacy could not be excluded.

Wiener (1935) also worked out the frequencies of the genes, in regard to this theory, and found that the frequencies of the six phenotypes recalculated from the frequencies of the genes closely approximated the observed frequencies. Thus it can be said that statistical considerations justify the acceptance of this theory.

As a result of the information given above it can be generally concluded that the theory of Thomsen, Friedenreich and Worsaae is fundamentally correct. However, exceptions to the theory cannot be ruled out, so that a final solution as to the exact basis of heredity must await further study.

AGGLUTINOGENS M AND N OF LANDSTEINER AND LEVINE

So far in this discussion it has been shown that there are six different divisions of human blood; namely those of "O, A, B and AB", and also the sub-groups of "A" and "AB". Recent studies by Landsteiner and Levine (1926) have shown that there exists in the red blood cells certain other agglutinable factors which are unrelated to "A" and "B". Thus there are at least two other divisions of human blood.

In 1926 Landsteiner and Levine found that when human blood was injected into certain immune sera of rabbits and this mixture was exhausted by certain other bloods it still retained agglutinins capable of acting on the majority of the four blood groups, while others were not agglutinated at all. These two factors, which were derived from such direct observation, were given the names of "M and N".

The above mentioned authors discovered that certain types of blood could be designated according to their possession of, or lack of, these types. The first division was found to be of the nature of "M+ N-" (blood containing "M" but lacking "N"), the second was of type "M- N+ (blood containing "N" but lacking "M"), the third was of M+ N+ (containing both "M" and "N"). Not a single blood lacking both "M" and "N" (M- N-") was found. Furthermore, the frequencies of the agglutinogens "M" and "N" were of such a nature that they must have been entirely un-

related to "A and B".

Hereafter, in this discussion, the types will be considered according to the agglutinogen present; that is "M", "N" and "MN". The lack of the agglutinogen is therefore not shown, but should be understood as being implied.

Heredity of the "M" and "N" Types. It has already been shown that Landsteiner and Levine first discovered the presence of these types in human blood. It was these same authors who supplied the theory which accounts for the heredity of these "M" and "N" types.

As a result of a study of sixty-four families with two hundred and eighty-six children, the above mentioned authors were able to demonstrate that the properties of "M" and "N" are inherited by means of a single pair of allelomorphic genes. Thus only three genotypes are possible; "MM", MN", and "NN". These, of course, correspond to the phenotypes "M", "MN" and "N". This theory also accounts for the lack of any blood bearing either "M" or "N". In the same manner the fact that an "MN" type results is explained by this theory through the assumption that neither of the genes "M" or "N" is dominant over the other. In regard to the homozygosity and heterozygosity of these types it is obvious that the "M" type ("M+ N-") and the "N" type ("M- N+") belong to the former, whereas "MN" is heterozygous and belongs to the latter. (Wiener, Zinsher, Selkowe, 1934).

As a result of this theory six different matings are

relative to "I" and "C".

Therefore, in this discussion, the term will be used to mean the relationship between "Personal" and "I", "I" and "C". The term of the equilibrium is therefore not static, it should be considered as being implied.

Figure 1 is that "P" and "I" types. In the diagram there are three lines and lines and further lines showing the presence of three types in human field. In the lower area interests are expressed the theory which represents the possibility of three "P" and "I" types.

In a people of a state of mind-flow Emotions also in material and mind-its relations, the above mentioned methods also in determining that the relationship of "P" and "I" are identified by means of a minor scale of attitudes. These only third relations are considered "P", "I", and "C". Note, of course, correlation to the identified "P", "I" and "C". This theory also indicates the lack of any three having either "P" or "I". In the same manner the "P" type is the type which is obtained in this theory showing the assumption that relations of the power "P" or "I" is included more the power. In regard to the good quality and attributes of the three types it is obvious that the "P" type ("I", "C") and the "I" type ("P", "C") belong to the theme, measure "C" is intermediate and belongs to the series. (Hilmer, Hilmer, Sullivan, 1969).

In a result of this theory the different matters are

possible. If the types of the parents are known it is a simple matter to determine what the types of the resulting children will be. For example, in a cross of "M" X "N", the former parent must have a genotype of "MM", and the latter parent must have a genotype of "NN". Thus, the "M" parent can produce germ cells containing only "M"; and the "N" parent, germ cells containing only "N". Thus, at the fusion of the gametes, the "M" and "N" will be united forming a zygote of the "MN" type. No other combination is possible. Likewise, in a mating of "MN" X "MN", all types of children are possible, since both parents are capable of producing germ cells of either "M" or "N". Thus, random combinations of these will produce "MM", "NN" or "MN". The other four matings can be analyzed in a similar manner from Table VI. This not only shows the results but also the number of each type expected from a total of one hundred offspring.

A summary of all the data observed shows that two rules should hold according to the theory advanced:

1. Agglutinogen "M" cannot appear in the blood of a child unless present in the blood of at least one of its parents. This rule holds for agglutinogen "N" as well.

2. A type "M" parent cannot give rise to a type "N" child, and a type "N" parent cannot give rise to a type "M" child. This rule follows from the fact that a type "M" individual is of genotype "MM" and thus can produce only germ cells bearing "M". Therefore, each child must contain at least

one "M" gene, and therefore, could not belong to genotype "NN". Similar reasoning holds for the reverse combination.

In the data published on the results of investigations on these types, there was one "exception" to the first law and seven "exceptions" to the second rule. The exceptions to the second rule can be accounted for by illegitimacy because in each case the parent involved was the father. If the theory was at fault the same exceptions should have been found in which the mother was implicated. "To date 6071 mother-child combinations have been examined and not once have the combinations, type "M" mother and type "N" child or type "N" mother and type "M" child been encountered." (Wiener, 1935, page 129)

It has been shown that for every two "exceptions" to the second rule, attributed to illegitimacy, one exception to the first rule is to be expected. Thus, the one "exception" noted in regard to the first rule can be reasonably assumed to be due to illegitimacy. (Wiener, 1935)

Statistical Considerations. In regard to statistical considerations it is possible to test whether the theory of Landsteiner and Levine is correct in regard to "M" and "N" by a study of agglutinogens "M" and "N" in mother-child combinations. The exact derivation of the formula used is given in Wiener (1935). This is based on the frequencies of the mother-child combinations in terms of the frequencies of the genes. (Formula "$M^4 + M^3 N = M^3 (M + N) = M^3$).

Application of this formula to actual observations has re-

sulted in complete agreement with expectancies. "As a result, therefore, of all studies made up to the present time, the theory of Landsteiner and Levine that the heredity of the agglutinogens "M" and "N" depends upon a single pair of allelomorphic genes, neither of which is recessive, is firmly established. The evidence in favor of the theory may be classified as follows:

1. Observation in Families

   a. Qualitative. (non-existence of true exceptions to the two laws of heredity).

   b. Quantitative.

2. Observations on Mothers and Children.

   a. Qualitative. (non-existence of a single combination of type "M" mother with type "N" child or vice-versa).

   b. Quantitative.

3. Analysis of Statistics in Population.

   a. Qualitative. (non-existence of the type "M-N-" among more than 20,000 specimens of blood studied up to the present time." (Wiener, 1935, page 135)

One important fact must be remembered when considering the "M" and "N" types: there are no natural agglutinins for "M" and "N" in human sera. Therefore, the transference of their agglutinogens plays no part in the selection of donors for blood transfusions. This, of course, is of a primary importance in its medical application, but it does not detract

from its medicolegal applications.

ANTHROPOLOGICAL INVESTIGATIONS

By means of serological tests, the proteins and cells of animals of different species can be separated and classified. The same idea has been tried in the classification of the different races of man. This led to a general idea that sera could be produced which would serve to differentiate the bloods of the different races. Thus far, all attempts along this line have been unsuccessful.

The factors controlling human blood are not restricted to any one race and consequently the presence or absence of the different blood groups, or of Landsteiner's "M" and "N" types cannot be used to distinguish any one race. However, one important fact has been gained in this study. That is, the frequency distribution of the agglutinogens varies in different races.

Racial Distribution of the Blood Groups. The first studies in this field were carried on by Hirschfeld and Hirschfeld during the World War. (Wiener, 1935). They examined and classified from five hundred to a thousand individuals of each race on the Macedonian Battle Front. The conclusions reached by these men are as follows:

1. Western Europe is predominantly group "A".

2. The Mongoloids and Negroids contain high percentages of group "B".

3. The Russians have an approximately even distribution

of "A" and "B". (In this latter group was also included the Turks, Arabs, and Jews).

The results cited above can be easily seen when the figures of L. and H. Hirschfeld have been reduced to the graph form. This is shown in Figure (E). Practically the same conclusions were reached by Landsteiner, 1931, who states that:

1. "A" is found more frequently in Northern Europe than is "B".

2. The condition is reversed in the Asiatic tribes, and in the American Indian the group is predominantly "O".

Snyder, 1926, worked on this problem and after a great deal of research arrived at the following conclusions:

1. "R", or the absence of both "A" and "B" exceeds in most people by more than fifty percent. This lack of "A" and "B" appeared to reach a minimum in the Ainus of Japan where it was 43.5%; and reached its maximum among the pure blooded American Indian. Here it was 95.5 percent. This "R", or lack of "A" and "B", is carried in a homozygous condition in all people of group "O". This factor may also be present in some of group "A" and "B".

2. The percent of group "A" and consequently the proportion of "A" agglutinogen appears to be at a maximum in the European type. It was highest among the Italians and lowest among the Icelanders.

3. Peoples of Eastern Europe and Asia Minor were classified as an "Intermediate Type" because these showed an in-

creased proportion of "A". It is only in this type that group "AB" reaches any degree of prominence.

4. Those of Asiatic Origin are classified as Hunan Types show a further increase in "B" agglutinogen and a corresponding decrease in "A" and "R". (Snyder, 1926)

From a comparison of both Hirschfeld and Snyder it can be seen that they both agree on the general distribution of the groups. Small discrepencies in their conclusions can be understood, and forgotten, when one considers the great amount of work entailed and also the amount of errors that are bound to creep in. As it is, minor details are of little importance because here, as in any other field, it is necessary to start first with large territories, and as the knowledge of the subject increases, so will small discrepencies disappear.

Origin of the Blood Groups. A question which is still undecided, although many theories have been put forth to answer it, is that of the origin of the various blood groups; that is, the manner in which the varying blood group distribution in the different peoples of the earth arose.

For example, it has been suggested in this paper that the predominance of group "O" is manifested in all people of the world and especially in the pure blooded American Indian. One theory explains this by assuming that properties of "A" and "B" appeared at a later date by mutation. If this theory was true we would have the answer to why the American Indian has practically no "A" nor "B". Obviously, the Indian Races must

have been separated from the main Asiatic trunk before the mutations arose.

Snyder, following his extensive work, drew conclusions as to the origin of the distribution of the groups. Naturally, his theory is based on his own work and seems to explain his results very thoroughly. (Wiener, 1935)

1. Agglutinogen "A" was a mutation originating in Western Europe. (Snyder, according to this, also seems to hold that the original group was "O").

2. Agglutinogen "B" was a second mutation arising in Eastern Asia (this seems to follow since the geographical intermediate group appears to manifest clearly the mixed condition in which both "A" and "B" are strongly represented).

It has been noted that whereas "B" becomes quite rare in the west (sometimes falling as low as three to five percent), the factor "A", although it does decrease from west to east, never becomes rare. Three theories have been offered to explain the phenomena. Which is correct cannot be answered with our present knowledge.

1. Mutation "B" occurred more recently than mutation "A", or mutation "B" occurred originally in fewer peoples than mutation "A". (Lambert, 1931).

2. "Migration eastward has taken place to a greater extent than migration westward in Eurasia". (Wiener, 1935)

3. An independent mutation of factor "A" occurred in Asia. (Lambert, 1931).

have been suggested from the main subsidy trend before the mobilization event.

Angus, following his subsidy work, that conditions in the origin of the distribution of the crops. Although the theory is based on the one hand and seems to explain a sudden year increase. (Hanson, 1967)

1. Agricultural "A" has a sudden subsidy in several years. (Hanson, presumed to hold, also seems to hold that the original group was "B").

2. Agricultural "B" has a special marketing system in which while seems to point about the government's intervention from figures to mark that change the price distribution to which both "A" and "B" are already responsive).

It was then found that whenever "B" changes price at the main marketing points in the so-called to free payment). the figure "A", although it does somewhat lag and to react, which seems to pay. These theories have been offered to explain the phenomena. Data to support either is contained with one previous hypothesis.

1. Agricultural "A" responses more rapidly than subsidies "B" or purchase "B" responses relatively in fact reaches from subsidy "A". (Hanson, 1967).

2. "Subsidies received can then drive to a smaller extent than supervision subsidies in general". (Hanson 1967)

3. An independent subsidies or labor "A" supported to data. (Hanson, 1967).

Wyman and Boyd (1935) on the other hand, point out that there are too many objections to the above mentioned theories to place any trust in their conclusions today. These objections are based on the fact that the same groups are spread over too wide a range to be adequately explained by the theories. They believe that the various distributions came into existence through mutations either after the various peoples arose, or where actually present in the anthropoid apes prior to their differentiation into man. The former appears to be more reasonable to these authors because it adequately explains the various difficulties for which all other theories fail to account. The latter statement cannot be denied at present due to the fact that certain substances have been found in the anthropoid apes which are indistinguishable from "A" and "B" found in man.

Distribution of "M" and "N". The first work on the racial distribution of agglutinogens "M" and "N" was performed by Landsteiner and Levine (1929). The most obvious facts observed by these co-workers was that there was a significant difference between Whites and the American Indian in regard to these properties. The same work was performed on other races (Germans, Italians, Japanese, Americans, Danes, Negroes), and there seemed to be the same or similar distributions of these characters.

By observing Landsteiner and Levine's statistics it seems that the American Indian is predominantly "M" and that the

Whites are predominantly "N". Landsteiner, himself, believes that there is a great possibility that the original Indian was one hundred percent "M" and that the small amount of "N" now found is due to the intermingling of the Indian and Whites.

The amount of work performed on the racial distribution of "M" and "N" has been very limited and until more and thorough studies have been made it is impossible to arrive at any conclusions that are worth considering.

As it is, the whole question of anthropology in blood groups has been entirely over emphasized. The knowledge of the subject is too small and spread out too far to warrant any definite conclusions. The theories advanced seem to crumble as new evidence is being presented. However, it can be used to great advantage by one who knows its possibilities and also knows its disadvantages.

MEDICOLEGAL APPLICATIONS

So far it has been shown that the agglutinogens A, B, M, and N of human blood are inherited in accordance with definite laws. Thus the problem of determining parentage by a consideration of blood relationships has become recognized throughout the world. Since the laws governing these relationships are constant then it would seem logical to suppose that facts flowing from the consideration of these laws would be gladly accepted in the court of law. However, this is not the case and the reason for its non-acceptance probably lies in that uncontrollable element in human nature which refuses to accept the facts as placed before it unless those same facts have been previously accepted by other groups. Thus we find that that even in the law courts of today new ideas are being placed on the table and ignored until some brave person can convince the people by actual use that those same facts are useful in balancing the scales of justice.

The United States appears to be one of those countries which fails to recognize the benefits and justice which knowledge of the blood groups has placed in its hands. The reason for this is probably the same as above: judges look for precedent before consenting to the introduction of scientific data as evidence.

Europe on the other hand has fallen into line and the

following countries have used this knowledge in a medicolegal line: Denmark, Danzig, Norway, Lithuania, Holland, Czechoslavakia, Sweden, Japan, Russia, Belgium, Ireland and Italy. (Wiener, 1935).

The picture in this country, although it is rather drab at present, appears to be taking on a brighter aspect when it is read in Wiener (1935) that after Dr. Karl Landsteiner had finished reading a report to the American Medical Association, dealing with the medicolegal applications of the blood groups, the above mentioned body unanimously passed the following motion:

"Resolved that the session organize a committee for the purpose of acquainting the suitable authorities in the legal profession with the existence and reliability of the blood grouping tests, so that statutes may be enacted authorizing courts to order individuals to submit to blood grouping tests when they are required, in those jurisdictions in which blood tests are not obligatory at present."

It has already been implied that knowledge of the blood groups is a vital force whereby the law could mete out justice both to the child and to the parents. Wiener (1935) has summarized cases of this nature under the following:

1. "A child is born in lawful wedlock and the husband denies paternity. The law presumes that all children in lawful wedlock are legitimate (in order to protect the interests of the child) unless it is proved that it was impossible for

the father to be the parent of said child. The courts allow, as proof of non-paternity, evidence of non-access, and sterility of the husband."

2. A child is born out of lawful wedlock and the man named by the mother as the father of her child, denies paternity.

3. Two new born infants have been accidentally interchanged in a hospital and it is desired to identify the parents of the infants. Or it is supposed that a wet-nurse has deliberately substituted her own child in the place of the one in her care so that her child will have the benefits of a better home.

4. "A woman has simulated pregnancy and child-birth, and now pretends that a certain child is her own in order to compel a man to marry her, or to obtain dower to her husbands estate (in jurisdiction where birth of same is a prerequisite to the right of dower), or in order that the child may become the heir to her husbands estate."

In answering these difficulties both the blood groups O, A, B, AB, and Landsteiner's M and N types are probably the most accurate. Of course, even by using such knowledge certain situations arise where no positive conclusions can be reached.

As has already been pointed out in the treatment of the four blood groups, the two following laws summarize the inheritance of these groups:

1. Agglutinogens "A" and "B" must be present in the blood

of one or both parents in order to appear in the blood of the child.

2. Parents belonging to groups "AB" cannot give rise to a group "O" child and a group "O" parent cannot give rise to a group "AB" child.

In Table 1 can be seen the exact relationship of the phenotypes and genotypes of these groups. Table 11 shows all possible crosses of these groups and also the results obtained from them. (In this table if the group is not designated in the list of possibilities then it is to be assumed that it is impossible.)

In order to get a clear picture of how the blood groups are used in regard to the four cases previously described an example of each will be given here. In all cases the actual statistics are fictitious with the one exception which was taken from Wiener, 1935.

Case Number 1.

Mrs. M. gives birth to a son. Mr. M. denies paternity. On examination Mrs. M. was found to be of group "O", Mr. M. group "A", and the child group "B".

The explanation of this case is a simple one. Since Mrs. M was of group "O" and her husband group "A", any legitimate child would have to be either "O" or "A". Under no circumstance is it possible for the child to be of "B" or "AB". This proves definitely that the husband, Mr. M, was not the father of the child and it also shows that the father was of group "B".

The latter statement is true because a cross of "O" and "B" can give only "O" and "B". In this case group "B" was inherited as a dominant from the father.

Case 11.

An unmarried woman accuses a certain man of the paternity of her child. All three were typed. Results: Mother belonged to group "O", putative father group "A", child group "B".

Since the child contained genes controlling group "B" it had to receive them from the father since the mother was of group "O". However, the accused man was of group "A". Therefore he was unjustly accused.

Case 111. (Wiener, 1935)

"After Mrs. W. had returned from the hospital, it was found that her baby had a label on its back with the name "B". The baby at the "B" home was found to bear the label with the "W". When the bloods were typed the following results were obtained:

1. Mr. W. - group "O" Mrs. W. - group "O"
2. Mr. B. - group "AB" Mrs. B. - group "O"
3. Baby labelled "W" - group "O". Baby labelled "B" - group "A".

This case can be solved in two ways.

1. Since Mr. B. belonged to group "AB" it was impossible for him to be the father of the child belonging to group "O". He could, however, be the father of the child belonging to group "A".

2. Since Mr. and Mrs. W. both belonged to group "O" they could not possibly have a child with a group other than group "O".

The final answer in this case is that the babies had been properly labelled but had accidentally been interchanged.

Case IV.

Woman of group "AB" claims that a child of Group "O" is her own.

In this case, since her husband was dead, the fact that she was of group "AB" is sufficient to show that she could not be the mother of this child. This is obvious from Table 11 which shows that no matter what group is crossed with group "AB", group "O" is never possible.

As can be easily seen, it is not always possible to establish the innocence of a man unjustly accused of paternity. The man may be of a group which could give the possible results, and still be innocent. It has thus become of exceeding importance to determine the exact chances of proving non-paternity in such cases.

Wiener (1935) claims that the possibility of establishing non-paternity in most races ranges between sixteen and nineteen percent. This is approximately one to six, or more, and denotes the whole range of the blood groups. In specific groups, however, it is found that a European of group "A" has only one chance in thirteen, whereas, the best chance is had in group "AB" where they are two to five. (Table 111).

Of course, in actual application such percentages would be exceedingly lower since some of the men would be justly accused. From Table IV it is found that this drops the average exclusions to approximately 8.2 percent. In other words, the chances are that at least one half of the fathers who could not prove their innocence by the blood groups would be unjustly accused.

In some cases it is not possible to determine the mother's group and, of course, the chances of proving non-paternity are very small. Wiener (1935) claims that the chances run as 4.7 percent; that is, approximately one in twenty.

One principle should be definitely understood: the blood groups are important in excluding paternity, but are absolutely useless when used for proving paternity. However, they can be used indirectly. If it is assumed that one of two men is the father of a certain child, and if one of them is excluded by the blood groups, it follows that the other is the father of the child.

Application of Agglutinogens M and N. The discovery of the types M and N and also their mechanism of heredity have been of considerable importance in the medicolegal applications of the blood groups. It has been previously shown that Landsteiner and Levine's theory in regard to these types seem to agree with all information that has been accumulated to date. Thus there is justification in using this theory in affiliation with the blood groups on such cases as have been already

been discussed. Therefore, in all cases where a decision is not possible from the results of the teste for "A" and "B", they can be supplemented by the tests for "M" and "N".

Naturally this lowers the percentages of errors that could be made if only the blood groups were used. In Table V can be seen the results that are possible between any combination of "M" and "N". Table VI not only verifies these results but also gives the percentage of offspring possible.

In the same fashion as in the blood groups the possibility of false accusation still holds true. The chances of proving non-paternity with the agglutinogens "M" and "N" are given in Table VII. As is shown here, a man falsely accused of paternity has approximately one chance in six (18.6 percent) of proving his innocence by this method. Men of type "MN" have no chance at all; men of either "M" or "N" have better than one chance in three. (Wiener, 1935)

This naturally leads us to the obvious fact that if both the blood groups and Landsteiner and Levine's "M" and "N" types are used together, the possibilities of proving non-paternity would be doubled. In other words, formerly a falsely accused man would have only one chance in six of proving his innocence, now he has one chance in three. Wiener (1935) has worked out the actual percentages upon the frequencies of the blood types in New York, and these percentages will be found in Table VIII.

Of course, the medicolegal applications of the agglutinogens "M" and "N" depends upon the two laws already mentioned in the

discussion of these types. The laws are reworded here in order to show how non-paternity can be proved from such cases.

1. If the child possesses an agglutinogen "M" or "N" which is not present in the blood of one or both parents, non-paternity is established. Wiener (1935) claims that one third of the exclusions probably belong to this class.

2. If either combination of type "N" man with type "M" child, or vice versa, is found, then non-paternity is established. This can easily be seen by referring to Table VI where it is shown that crosses between "M" and "M" and also between "M" and "N" will never produce a child with type "N". It also shows that any cross between "M" and "N" will never produce type "M" in the offspring.

An actual case is cited by Wiener (1935) which adequately explains the two above rules. "After eight years of married life, during which time she had frequent intercourse with her husband, but had failed to become pregnant, Mrs. X. met and fell in love with Mr. Y. During the ensuing five years, three children were born." The people involved reached an understanding and tried to determine the fathers of these children.

Blood tests showed:

Blood of	Group	Type
Husband	O	MN
Lover	A	N
Wife	O	MN
First Child	O	MN
Second Child	A	N

Blood of	Group	Type
Third Child	A	N

"It is obvious that the husband could not have been the father of the third child (belonging to group "A"), since both he and his wife belonged to group "O". On the other hand, since a type "N" man cannot give rise to a type "M" child, the lover could not be the father of the second child. By means of these tests, therefore, it has been proved indirectly that the husband is the father of the second child, and the lover the father of the third child. No decision can be rendered concerning the first child." (Wiener, 1935, page 197).

In regard to the interchanging of infants, a solution is possible in forty percent of the cases when the agglutinogens are tested. However, the figure is almost doubled when both the blood groups and the "M" and "N" types are referred to. The exact figure in this case is close to seventy percent.

Of course, since the discovery of Landsteiner "M" and "N" types, and since this gives more chances for an unjustly accused man to prove his innocence, a great many cases have been reopened. The results show that the theoretical claims were justified because they proved that some men were falsely accused through the evidence of only the blood group tests.

Here again the United States is slow in making use of such evidence. However, it can be said that this country is gradually being won over to the importance of such evidence. This was shown quite recently where a man in New Jersey was

granted a divorce on such evidence as was supplied by the blood group tests.

So far in this discussion of the medicolegal applications of the blood groups only those cases involving the determination of paternity have been considered. This, however, does not mean that the blood groups can be applied only to those cases. Hooker and Boyd (1934) have examined other ways in which the blood groups have been of service in the righting of wrongs and in the freeing of innocent people.

The most important of these methods discussed by these authors is that of blood stains. In a great many cases it is possible to exonerate a man accused of murder or some other crime by checking his blood with that of some blood stain which has been proved to have been left by the guilty person. Here, as in all other cases in which the blood groups play an important part, the innocence of a person can be proved by the use of such methods but the guilt of a person can not be based entirely on them.

Naturally some innocent person would not be able to prove his innocence due to the fact that his blood maybe of the same type as that of the stain. Thus it becomes extremely important to know the exact chances of proving the innocence of an unjustly accused person. Hooker and Boyd (1934) claim that the chances of exonerating an innocent man under these conditions would be approximately three to five. These conclusions are based only on the fact that "A" and "B" are used. If the "M"

and "N" types of Landsteiner and Levine are used in conjunction with them the chances of proving a persons innocence would be doubled.

Cigarette stubs which have been proved to be directly connected with a crime have also supplied means whereby the blood groups can be used in a medicolegal manner. This is due to the fact that the blood groups can be identified by examining the saliva present in the stub.

A third type in which the blood groups are capable of playing an important part is found in the examination of seminal fluid which has been deposited during an attempted rape. Of course, in this case it is generally applied in the interest of an innocent man accused of the crime.

SUMMARY

From earliest times the exact composition of blood has been of interest to mankind. The morphological species characteristics and individual differences have been know for centuries but it was not until comparatively recent times that the biochemical differences were recognized.

Landois, during the nineteenth century, investigated the causes of agglutination which resulted from infusion of human blood into other individuals. However, it was not until 1900 that Landsteiner observed the differences between normal individuals belonging to the same species. This man, with the help of von Decastello and Sturle, finally divided all human beings into four distinct groups. This division was based on the fact that when serum of one individual was mixed with the erythrocytes of another, agglutination was apt to occur. The final answer as to why the agglutination took place led to the founding of the four blood groups which are recognized today by the International Nomenclature (O, A, B, AB).

In 1925 the exact mechanism controlling the heredity of these groups was postulated by Bernstein. Other scientists also presented theories but these did not agree with the facts, as was later shown by detailed investigations. Bernstein's theory, which postulates triple allelomorphs A, B, and R, not only agrees with the facts but also coincides with the statis-

tical evidence on the frequencies of these genes.

In 1910 von Dungern and Hirschfeld proved definitely that there were sub-groups of A and AB of the original four blood groups. The hereditary nature of these sub-groups was practically answered in 1930 by Thomsen, Friedenreich, and Worsaae. This theory postulated four allelomorphic genes instead of three; namely, A_1, A_2, B and R. This did not change the fundamental principles of Bernstein's theory. Whether or not this theory is actually correct cannot be said at the present time. Inconsistencies are still being found and, until further evidence can be produced, Thomsen's theory must be accepted only with reservations.

A further division of the blood was made by Landsteiner and Levine in 1928 when they discovered the existence of the agglutinogens M and N. These men also supplied the theory accounting for the inheritance of these types. This theory postulates a single pair of allelomorphic genes, M and N. The exactness of this theory is attested to by the fact that not one true exception has been found contrary to the laws resulting from it.

No fitting ending, nor statement that adequately expresses the importance of the blood groups, can be applied here other than the words of (Wiener, 1935):

"The manifold applications of all this work in biology and in clinical and legal medicine prove that it is not merely of academic interest. The application of the Landsteiner blood

groups O, A, B, and AB, for the selection of blood donors has made blood transfusion a safe procedure, and has undoubtedly saved thousands of lives. In forensic medicine this knowledge has been applied for the identification of blood stains, and for the determination of non-paternity. Data have been collected by studies of blood groups in the various races which may prove of value to anthropology. Its contribution to serology has been to increase our understanding of the nature of the cellular antigens. The subject should therefore be of interest not only to the immunologist, but also to the physician, the lawyer, the geneticist, and the anthropologist."

TABLE 1

Blood Group	Possible Genetic Formulae	
O	OO	aabb
A	OA,AA or	AAbb, Aabb
B	OB,BB	aaBB, aaBb
AB	AB	AABB, AaBB
		AABb, AaBb

From: Lambert, W. V. Scientific Monthly. 33:40+41. 1931.

TABLE 11

Blood Groups of Parents	Possible Blood Groups in Children
O X O	O
O X A	O, A
O X B	O, B
O X AB	A, B
A X A	O, A
A X B	O, A, B, AB
A X AB	A, B, AB
B X B	O, B
B X AB	A, B, AB
AB X AB	A, B, AB

From: Lambert, W. V. Scientific Monthly. 33:42. 1931.

TABLE III

Chances of Proving non Paternity with the Blood Groups

	Frequencies of Groups				Percent Exclusions; Putative Father in Group				
	B	A	B	AB	O	A	B	AB	un-known
European (and American)	39	43	12	6	23.5	7.7	14.6	39.9	16.3
"Maximum"*	31.3	29.6	29.6	9.7	29	13.4	13.4	31.1	20

*This is a theoretical population giving maximum chances of excluding paternity.
From: Wiener (1935)

TABLE IV

MEDICOLEGAL APPLICATION OF BLOOD GROUPING

Country	Number of Cases	Paternity Exclusions	Percentage Exclusions
Germany	4519	353	7.8
Austria	700	63	9.0
Danzig	600	39	6.5
Denmark *	50	6	12.0
Denmark *	500	64	12.8
Sweden	259	17	6.6
Norway			
Switzerland	37	4	10.8
Lithuania			
Total	6665	546	8.2

*Different Authorities

From: Wiener (1935) (After Levine)

TABLE V

AGGLUTINOGENS M AND N IN PARENTS AND CHILDREN

Types of Parents	Types of children Possible	Types of Children Not Possible
1. MN X MN	M, N, MN	
2. MN X N	N, MN	M
3. MN X M	M, MN	N
4. M X N	MN	M, N
5. N X N	N	M, MN
6. M X M	M	N, MN

From: Wiener, A. S. Scientific Monthly. 40: 323-31. 1935.

TABLE VI

HEREDITY OF THE AGGLUTINOGENS M AND N

Marriages	Progeny to be Expected		
	M+ M+	M+ N-	M- N+
M+ N+ X M+ N+	50	25	25
M+ N+ X M- N+	50	0	50
M+ N+ X M+ N-	50	50	0
M+ N- X M- N+	100	0	0
M+ N- X M+ N-	0	100	0
M- N+ X M- N+	0	0	100

From: Landsteiner, Karl. Science. N.S. 73. 407. , 1931.

TABLE VII

CHANCES OF PROVING NON PATERNITY WITH AGGLUTINOGENS M AND N

Racial Type	Frequencies of Types			Percent Exclusions: Putative Father in Type			
	M	N	MN	M	N	MN	Un-known
European	29.2	21.2	49.6	34.6	40.6	0	18.6
Maximum*	25	25	50	37.5	37.5	0	18.75

*This is a theoretical population giving the maximum chances of proving non-paternity.

From: Wiener (1935).

TABLE VIII

CHANCES OF PROVING NON-PATERNITY WITH THE AGGLUTINOGENS

A, B, M and N.

Group	O			A			B			AB			UN-
Type	M	N	MN	M	N	MN	M		MN	M	N	MN	KNOWN
Chances (percent)	50.0	54.6	23.5	39.6	45.1	7.7	44.1	49.3	14.6	60.7	64.3	39.9	31.9

FROM: WIENER (1935).

TABLE IX

PHENOTYPES AND GENOTYPES OF SUB-GROUPS

Phenotype	Genotype	
	Homozygous	Heterozygous
O	RR	———
A_1	A_1 A_1	A_1 R and A_1 A_2
A_2	A_2 A_2	A_2 R
B	BB	BR
A_1 B	———	A_1 B
A_2 B	———	A_2 B

From: Wiener (1935)

TABLE X

BERNSTEIN'S THEORY

Phenotype	Genotype	
	Homozygous	Heterozygous
AB	———	AB
A	AA	AR
B	BB	BR
O	RR	———

From: Wiener (1935)

TABLE XI

COMPARISON OF THE TWO THEORIES OF HEREDITY OF THE BLOOD GROUPS

Groups of Parents	Groups of Children (v. Dungern and Hirschfeld)	Groups of Children (Bernstein)
1. O X O	O	O
2. O X A	O, A	O, A
3. O X B	O, B	O, B
4. A X A	O, A	O, A
5. A X B	O, A, B, AB	O, A, B, AB
6. B X B	O, B	O, B
7. O X AB	O, A, B, AB	A, B
8. A X AB	O, A, B, AB	A, B, AB
9. B X AB	O, A, B, AB	A, B, AB
10. AB X AB	O, A, B, AB	A, B, AB

From: Wiener (1935)

TABLE XII

BERNSTEIN'S THEORY

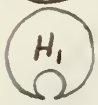
Phenotype	Genotype	
	Homozygous	Heterozygous
AB		AB
A	AA	AR
B	BB	BR
AB	RR	

From: Wiener (1935)

FIGURE A

EHRLICH SYMBOLS

Blood Cells Lacking Agglutinogens



Blood Cells Possessing Agglutinogen H_1

Immune Agglutinin h_1

Blood Cells Possessing Agglutinogen H_2

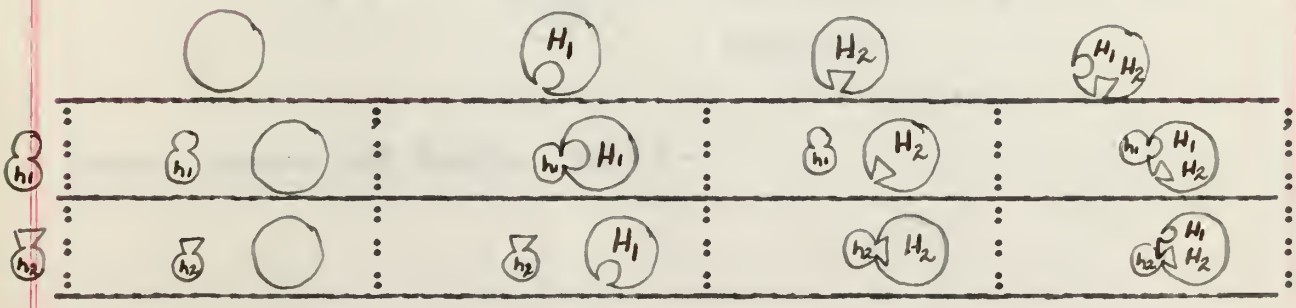
Blood Cells Containing Both H_1 and H_2

Immune Agglutinin h_2

Indicates agglutination or neutralization reaction between H_1 agglutinogen in blood cells and h_1 agglutinin in a serum.

From: Keeler and Castle (1934)

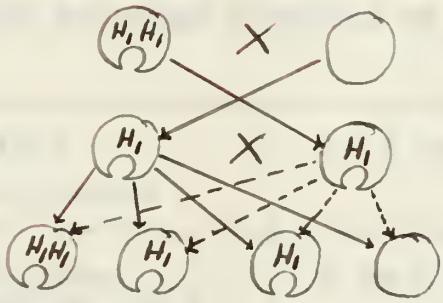
FIGURE B



From: Keeler and Castle (1934)

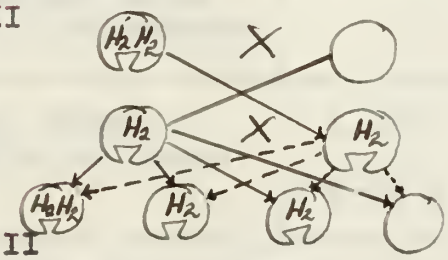
FIGURE C

CROSS I



This cross proves definitely that H is a dominant Unit Character. Ratio of 1:2:1.

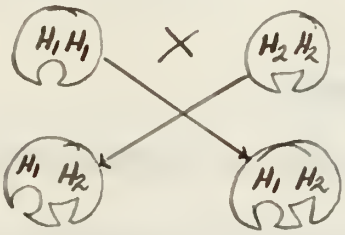
CROSS II



Proves H_2 is a dominant Unit Character. Ratio of 1:2:1.

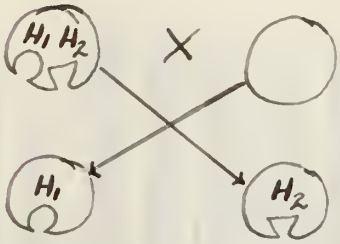
CROSS III

CROSS III



Crossing two hemozygous animals of H_1 and H_2 gives only a heterozygous animal. Proves H_1 and H_2 are autonomous.

CROSS IV



Indicates that such H_1 H_2 individuals transmit H_1 and H_2 in separate gametes. Therefore, H_1 and H_2 are allelomorphics.

From: Keeler and Castle (1934)

FIGURE D

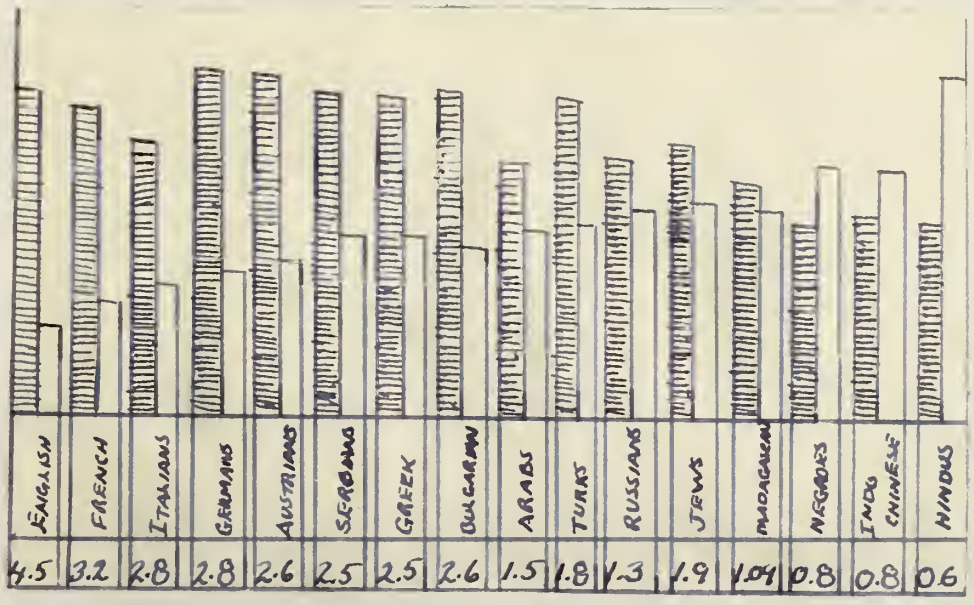
THREE PROPOSED THEORIES ON HEREDITY OF BLOOD GROUPS

Triple Allelomorphs	A, B or R A, B, or R
Two Independent pairs of Allelomorphs	A or a A or a B or b B or b
Two Linked Pairs of Genes	A or a A or a B or b B or b

From: Wiener (1935)

FIGURE E

DISTRIBUTION OF THE AGGLUTINOGEN A AND B



From: Wiener (1935)

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